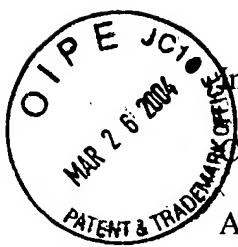


03-29-04

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



In re application of:  
Cynthia B. Robinson, et al.  
Appl. No. 10/698,079

Filed: October 29, 2003

For: COMBINATION OF  
DEHYDROEPIANDROSTERONE OR  
DEHYDROEPIANDROSTERONE-  
SULFATE WITH AN ANTICHOLINERGIC  
BRONCHODILATOR FOR TREATMENT  
OF ASTHMA OR CHRONIC  
OBSTRUCTIVE PULMONARY DISEASE

Art Unit: 1646  
Examiner: Not Yet Assigned  
Confirmation No.: 9159  
Atty. Docket: 05882.0068.NPUS01

**Information Disclosure Statement**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith. It is further understood that the Examiner will consider information that had been cited by or submitted to the U.S. Patent and Trademark Office in a prior application relied on under 35 U.S.C. § 120.  
1138 OG 37, 38 (May 19, 1992).

Applicants have checked the appropriate boxes below.

- 1. This Information Disclosure Statement is being filed;
  - a. Within three months of the U.S. filing date of a national application other than a continued prosecution application under §1.53(d);
  - b. Within three months of the date of entry of the national stage as set forth in §1.491 in an international application;
  - c. Before the mailing date of a first Office Action on the merits;
  - d. Before the mailing of a first Office Action after filing of a request for continued examination under § 1.115.

No statement under 37 C.F.R. § 1.97(e) or fee is required.

or;

- 2. This Information Disclosure Statement is being filed after the period specified in paragraph 1(a)-1(d) above, but before the mailing date of a Final Rejection or Notice of Allowance, or action that otherwise closes prosecution in the application, and
  - a. I hereby state that each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement. 37 C.F.R. § 1.97(e)(1), or
  - b. I hereby state that no item of information in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to my knowledge after making reasonable inquiry, no item of information contained in this Information Disclosure Statement was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Information Disclosure Statement. 37 C.F.R. § 1.97(e)(2), or

- c. Attached is our Check No. \_\_\_\_\_ in the amount of \$ \_\_\_\_\_ in payment of the fee under 37 C.F.R. § 1.17(p).
3. This Information Disclosure Statement is being filed more than three months after the U.S. filing date and after the mailing date of a Final Rejection or Notice of Allowance, but on or before payment of the Issue Fee. Attached is our Check No. \_\_\_\_\_ in the amount of \$ \_\_\_\_\_ in payment of the fee under 37 C.F.R. § 1.17(i), and
- a. I hereby state that each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Information Disclosure Statement. 37 C.F.R. § 1.97(e)(1), or
- b. I hereby state that no item of information in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to my knowledge after making reasonable inquiry, no item of information contained in this Information Disclosure Statement was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Information Disclosure Statement. 37 C.F.R. § 1.97(e)(2).
4. Relevance of the non-English language document(s) is discussed in the present specification.
5. The document(s) was/were cited in a corresponding foreign application. An English language version of the foreign search report is attached for the Examiner's information.
6. A concise explanation of the relevance of the non-English language document(s) appears below:
7. The Examiner's attention is directed to co-pending U.S. Patent Application No. \_\_\_\_\_, filed \_\_\_\_\_, which is directed to related technical subject matter. The identification of this U.S. Patent Application is not to be construed as a waiver of secrecy as to that application now or upon issuance of the present application as a patent. The Examiner is respectfully requested to consider the cited application and the art cited therein during examination.
8. Copies of the documents were cited by or submitted to the Office in Application No. \_\_\_\_\_, filed \_\_\_\_\_, which is relied upon for an earlier filing date under 35

Applicants: Cynthia B. Robinson, *et al.*  
Appl. No. 10/698,079

U.S.C. § 120. Thus, copies of these documents are not attached. 37 C.F.R. § 1.98(d).

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and to indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 08-3038 referencing docket number 05882.0068.NPUS01.

Respectfully submitted,

Date: March 26, 2004



Albert P. Halluin (Reg. No. 25,227)  
Robin C. Chiang (Reg. No. 46,619)

**HOWREY SIMON ARNOLD & WHITE, LLP**  
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(650) 463-8109

## LIST OF REFERENCES CITED BY APPLICANT

(Use several sheets if necessary)

PTO FORM 1449

ATTY. DOCKET NO.

02486.0068.NPUS01

APPLICATION NO.

10/698,079

APPLICANT

Cynthia B. Robinson, et al.

FILING DATE

October 29, 2003

GROUP

1646

U.S. PATENT DOCUMENTS							
*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	1.	3,505,337	Apr. 1970	Zeile et al.			
	2.	4,208,423	Jun. 1980	Pfister			
	3.	4,385,048	May 1983	Mygind et al.			
	4.	4,393,066	Jul. 1983	Garrett et al.			
	5.	4,499,064	Feb. 1985	Shive			
	6.	4,575,498	Mar. 1986	Holmes et al.			
	7.	4,628,052	Dec. 1986	Peat			
	8.	4,920,115	Apr. 1990	Nestler et al.			
	9.	4,931,441	Jun. 1990	Lawrence			
	10.	4,985,443	Jan. 1991	Montes			
	11.	5,021,417	Jun. 1991	Prost			
	12.	5,059,595	Oct. 1991	Le Grazie			
	13.	5,077,284	Dec. 1991	Loria et al.			
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	23.	5,407,927	Apr. 1995	Morales et al.			

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<b>LIST OF REFERENCES CITED BY APPLICANT</b> <i>(Use several sheets if necessary)</i>				ATTY. DOCKET NO. <b>02486.0068.NPUS01</b>	APPLICATION NO. <b>10/698,079</b>
<b>PTO FORM 1449</b>				APPLICANT <b>Cynthia B. Robinson, et al.</b>	
				FILING DATE <b>October 29, 2003</b>	GROUP <b>1646</b>

24.	5,489,581	Feb. 1996	Daynes et al.					
25.	5,527,789	Jun. 1996	Nyce					
26.	5,532,230	Jul. 1996	Daynes et al.					
27.	5,538,734	Jul. 1996	Le Grazie					
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29.	5,603,918	Feb. 1997	McNamara					
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33.	5,703,063	Dec. 1997	Chasalow, et al.					
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36.	5,859,000	Jan. 1999	Dowell et al.					
37.	5,861,391	Jan. 1999	Yen et al.					
38.	5,948,434	Sep. 1999	Labrie					
39.	5,955,058	Sep. 1999	Jager et al.					
40.	6,087,351	Jul. 2000	Nyce					
41.	6,093,706	Jul. 2000	Zeligs					
42.	6,299,861	Oct. 2001	Banholzer et al.					
43.	6,455,028	Sep. 2002	Wulffhart et al.					
44.	6,455,524	Sep. 2002	Bozung et al.					
45.	2002/0042401	Apr. 2002	Ferguson et al.					
46.	2003/0013772	Jan. 2003	Murphy et al.					
47.	2003/0138434	Jul. 2003	Campbell et al.					
48.	2003/0139331	Jul. 2003	Martin et al.					

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		FILING DATE <b>October 29, 2003</b>	GROUP <b>1646</b>

<b>FOREIGN PATENT DOCUMENTS</b>								
*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
49.	X	EP 0 418 716 B1		Europe				
50.	f	WO 93/16704		PCT				
51.	X	WO 96/16680		PCT				
52.	X	WO 97/48367		PCT				
53.	X	WO 98/03180		PCT				
54.	X	WO 00/54763		PCT				
55.	f	WO 01/015745		PCT				
56.	X	WO 02/069955		PCT				
57.	f	WO 02/85296		PCT				
58.	f	WO 03/072572		PCT				
59.	X	WO 04/014293 A2		PCT				

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60.	X	Araneo et al., "Dehydroepiandrosterone Reduces Progressive Dermal Ischemia Caused by Thermal Injury", <i>J. Surg. Res.</i> 59(2):250-62 (1995).
61.	f	Bonnett et al., "Dehydroepiandrosterone (DHEA) prevents and reverses chronic hypoxic pulmonary hypertension," <i>PNAS</i> 100(16):9488-93 (2003).
62.	X	Budavari, <i>The Merck Index</i> 11 <sup>th</sup> ed., 1989, pp. 660-661, monograph 4141.
63.	X	Coleridge et al., "Intravenous aminophylline confers no benefit in acute asthma treated with intravenous steroids and inhaled bronchodilators", <i>Aust. N.Z. J. Med.</i> 23:348-54 (1993).
64.	X	Dashtaki et al., " Dehydroepiandrosterone and Analogs Inhibit DNA Binding of AP-1 and Airway Smooth Muscle Proliferation <sup>1</sup> ," <i>J. Pharmacol. Exp. Thera.</i> 285(2):876-83 (1998).
65.	X	Dompeling et al., "Treatment with Inhaled Steroids in Asthma and Chronic Bronchitis: Long Term Compliance and Inhaler Technique", <i>Family Practice</i> 9(2):161-6 (1992).
66.	X	Dunn, et al., "Dehydroepiandrosterone sulphate concentrations in asthmatic patients: pilot study," <i>N.Z. J. Med.</i> 97(768):805-8 (1984).

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No Received 9/04

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67. <input checked="" type="checkbox"/>	Duplantier, et al., Novel pharmacological approaches to the treatment of asthma: status and potential of therapeutic classes", <i>DDT</i> 1(5):199-207 (1996)
68. <input checked="" type="checkbox"/>	Dworski et al., "Conspectus: Inhaled Steroids in Asthma", <i>Comprehensive Therapy</i> , 18:3 (1992).
69. <input checked="" type="checkbox"/>	Fehér et al., "Adrenocortical Function in Bronchial Asthma", <i>Acta Medica Hungarica</i> 40(2-3):125-32 (1983).
70. <input checked="" type="checkbox"/>	Fehér, et al., "Dehydroepiandrosterone Therapy of Patients with Corticosteroid Dependent Bronchial Asthma," <i>Natl. Institute of Rheumatism and Physiotherapy, in XIII Congress of the European Academy of Allergology and Clinical Immunology</i> , eds. (Saba, et al., Debrecen Hungary (1986).
71. <input checked="" type="checkbox"/>	Hampl et al., "Dehydroepiandrosterone sulphate reduces chronic hypoxic pulmonary hypertension in rats," <i>J. Eur. Respir.</i> 21:862-5 (2003).
72. <input checked="" type="checkbox"/>	Holzmann et al., "Therapy of Psoriasis with Dehydroepiandrosterone-Enanthate. II. Intramuscular Depot Application of 300 mg", <i>Arch. Dermatol. Forsch.</i> 247(1):23-8 (1973) (German with English Abstract).
73. <input checked="" type="checkbox"/>	Hummel et al., "Comparison of oral-steroid sparing by high-dose and low-dose inhaled steroid in maintenance treatment of severe asthma", <i>The Lancet</i> , 340(8834/8835):1483-7 (1992).
74. <input checked="" type="checkbox"/>	Inn, "Treatment of COPD Bronchodilator Muscarinic Antagonist", <i>Drugs of the Future</i> 25(7):693-9 (2000)
75. <input checked="" type="checkbox"/>	Itagaki et al., "Effect of Cortisol on the Release of Human Decidual", <i>Caplus</i> , 114875 (1991) (Japanese with English Abstract).
76. <input checked="" type="checkbox"/>	Koó et al., "Our experiences with Dehydroepiandrosterone Therapy in Steroid-Dependent Intrinsic Bronchial Asthma", <i>Orvosi Hetilap</i> 128(38):1995-7 (1987) (Hungarian).
77. <input checked="" type="checkbox"/>	Koó et al., "Our experiences with Dehydroepiandrosterone Therapy in Steroid-Dependent Intrinsic Bronchial Asthma ", <i>Orvosi Hetilap</i> 128(38):1995-7 (1987) (English translation).
78. <input checked="" type="checkbox"/>	Lejeune, "Pathogenesis of Mental Impairment in Trisomy 21", <i>Annales de Génétique</i> , 92:27643 (1996) (French with English Abstract).
79. <input checked="" type="checkbox"/>	Mileva et al., "Androstenedione, DHEA sulfate, cortisol, aldosterone and testosterone in bronchial asthma patients", 07608054 (1990) (Russian with English Abstract).
80. <input checked="" type="checkbox"/>	Nakagawa, et al., "The Properties of Water of Crystallization of Sodium Prasterone Sulfate," <i>Chem. Pharm. Bull</i> 29(5):1466-9 (1981)
81. <input checked="" type="checkbox"/>	Nakagawa, et al., "The Grinding and Drying on the Solid State Stability of Sodium Prasterone Sulfate," <i>Chem. Pharm. Bull</i> 30(1):242-8 (1982)

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82. <input checked="" type="checkbox"/>	Pashko <i>et al.</i> , "Inhibition of 7,12-dimethylbenz(a)anthracene-induced Skin Papillomas and Carcinomas by Dehydroepiandrosterone and 3-beta-methylandrost-5-en-17-one in mice", <i>Cancer Res.</i> 45(1):164-6 (1985).
83. <input checked="" type="checkbox"/>	Peeters <i>et al.</i> , "Differences in Purine Metabolism in Patients with Down's Syndrome", <i>J. Intellect. Diabil. Res.</i> 37:471 (1993). Abstract.
84. <input checked="" type="checkbox"/>	Reed, "Aerosol Steroids as Primary Treatment of Mild Asthma", <i>New England J. Med.</i> , 325(6):425-6 (1991).
85. <input checked="" type="checkbox"/>	Rowe <i>et al.</i> , "Effectiveness of Steroid Therapy in Acute Exacerbations of Asthma: A Meta-analysis", <i>Amer. J. Emergency Med.</i> , 10(4):301-10 (1992).
86. <input checked="" type="checkbox"/>	Sasaki <i>et al.</i> , "Cervical Ripening with Dehydroepiandrosterone Sulphate", <i>Br. J. Obstet. Gynaecol.</i> 89(3):195-8, (1982).
87. <input checked="" type="checkbox"/>	Sciarrà <i>et al.</i> , "Aerosols", Remington's Pharmaceutical Sciences, 18 <sup>th</sup> ed. (1990), Eds. Gennaro <i>et al.</i> , pp. 1873-5 and 1694-1712.
88. <input checked="" type="checkbox"/>	Sharma <i>et al.</i> , "Screening of potential chemopreventive agents using biochemical markers of carcinogenesis", <i>Cancer Res.</i> 54(22):5848-55 (1994).
89. <input checked="" type="checkbox"/>	Shomali, "The Use of Anti-Aging Hormones. Melatonin. Growth Hormone, Testosterone, and Dehydroepiandrosterone: Consumer Enthusiasm for Unproven Therapies", <i>Md. Med. J.</i> 46(4):181-6 (1997).
90. <input checked="" type="checkbox"/>	Sonka <i>et al.</i> , "Gout and Dehydroepiandrosterone: 3. DHEA Administration", <i>Endokrynologia Polska</i> 24(3):209-18 (1973).
91. <input checked="" type="checkbox"/>	Sur <i>et al.</i> , "Double-blind trial pyridoxine (vitamin B6) in the treatment of steroid-dependent asthma", <i>Ann. Allergy</i> , 70:147-52 (1993).
92. <input checked="" type="checkbox"/>	Schwartz <i>et al.</i> , "Inhibition of 7,12-dimethylbenz[a]anthracene- and urethan-induced lung tumor formation in A/J mice by long-term treatment with dehydroepiandrosterone," <i>Carcinogenesis</i> 2(12):1335-7 (1981)
93. <input checked="" type="checkbox"/>	Van de Graaf <i>et al.</i> , "Respiratory Membrane Permeability and Bronchial Hyperreactivity in Patients with Stable Asthma: Effects of Therapy with Inhaled Steroids", <i>Bronchial Asthma and Respiratory Membrane Permeability</i> 143:362-8 (1991).
94. <input checked="" type="checkbox"/>	Van Vollenhoven <i>et al.</i> , "Dehydroepiandrosterone in SLE. Results of a Double-Blind, Placebo-Controlled, Randomized Clinical Trial.", <i>Arthritis Rheum.</i> 38(12): 1826-31 (1995).
95. <input checked="" type="checkbox"/>	Wolkowitz <i>et al.</i> , "Dehydroepiandrosterone Treatment of Depression", <i>Biol. Psychiatry</i> 41(3):311-8. (1997).

*DOC Ne Cited*

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